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USSR TRENDS IN RESEARCH ON PROTEINS

One of the most interesting developments in USSR research on proteins is a series of investigations on the resynthesis of hydrolyzed proteins under pressure. The investigations were carried out at the Leningrad Physicotechnical Institute, Academy of Sciences USSR, under the direction of Prof S. Ye. Bresler.(1) Work on the subject has been conducted by Bresler's group since 1947. Bresler found that when a dilute protein hydrolyzate to which a small quantity of a proteolytic enzyme such as trypsin, chymotrypsin, or pepsin has been added is subjected to a sufficiently high pressure (5,000-10,000 atm), the original protein which has been split to produce the hydrolyzate is resynthesized. Furthermore, in this resynthesis all intermediate stages are skipped: protein molecules which have the original molecular weight are formed immediately. The physical properties of the original protein are restored and its immunological properties, which are lost on hydrolysis, are fully regained after resynthesis under pressure. This was established in experiments in which equine, bovine, or human serum albumin, and equine gamma-globulin served as substrates. Similar experiments were carried out with insulin and muscle aldolase, [myogen A?]. In the case of the typical enzyme muscle aldolase and the typical hormone insulin, the enzymatic and hormone activity respectively were not restored completely, but only to the extent of 10%.(1,2)

After the group headed by Bresler had established that the macrostructure of immunologically active proteins which have been hydrolyzed is fully restored by resynthesis under pressure in the presence of a proteolytic enzyme, A. G. Pasynskiy and D. L. Talmud carried out experiments aimed at the modification of such proteins. On treating unhydrolyzed natural protein under pressure with an excess of phenylalanine in the presence of a proteolytic enzyme, they found that some of the tyrosine of the original protein was replaced with phenylalanine. This and other observations established that proteins can be modified at will within certain limits (subjected to "directed modification") during the process of resynthesis. The conclusion that proteins can be modified in this manner has far-reaching implications from the standpoint of immunology in particular, and of applied chemistry and biochemistry in general. (2)

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From the fact that his hydrolyzates of antigenic proteins (albumin which subsequent to hydrolysis contain polypeptides consisting of 7-8 amino-acid residues), in addition to being incapable of producing active immunity in animals, do not produce passive immunity either, Bresler concluded that haptenes are absent in these hydrolyzates. On subjecting to pressure resynthesis a mixture of the hydrolyzates of bovine and equine serum albumin in the optimum proportion of 3 to 1, Bresler obtained a degree of resynthesis amounting to 30-35%. He found that macromolecules corresponding in size to those of the original albumins were not resynthesized: only smaller polypeptides were present. Although these polypeptides did not produce active immunity, they did react with antibodies already present in the body of the animal, i.e., they had haptenic activity.(3)

Using Bresler's method, S. Ye. Manoylov prepared at the Institute of Roentgenology and Cancer synthetic substances of a new type in which nucleic acids are combined with amino acids. The work in question clarified the nature of the bonds present in nucleoproteids.(4)

Closely connected with research on antigenically active proteins is work on the chemical composition of the so-called complete antigens isolated from bacteria. Work is being conducted in the USSR on the isolation and chemical detoxification of complete antigens with the view of applying them in the prophylaxis of infectious diseases. On the basis of a review of USSR and Western work in this field, V. I. Ivanov, who is active in research of this type, arrived at the conclusion that the present state of work on this subject opens up possibilities of isolating and using complete antigens on a wide scale.(5)

As indicated by a recent review of work on the artificial production outside of the organism of antibodies counteracting natural and artificial antigens, some interest in this subject from the standpoint of eventual practical applications exists in the USSR. However, the article in question is more concerned with establishing Russian and USSR priorities in this field and criticizing L. Pauling's work on the subject than with giving an informative review of recent research done in the USSR.(6)

A considerable amount of research on the chemistry and physical chemistry of immunologically active and inactive blood proteins has been done by the Central Order of Lenin Institute of Hematology and Blood Transfusion and the local institutes of blood transfusion which are affiliated with it. The Physicochemical Institute of the Academy of Sciences USSR participated in some of this work.(7) Research on the assimilation of intravenously administered heterogeneous proteins has been conducted in the USSR both from the standpoint of using heterogeneous proteins (e.g., specially treated cattle serum) as blood substitutes and with the view of investigating the mechanism of the antigenic action of parenterally administered proteins. An interesting theory has been advanced by I. P. Razenkov to the effect that intravenously administered proteins (e.g., serum globulins and albumins) are released into the gastrointestinal tract and split there into individual amino acids (i.e., digested) prior to final resorption into the blood stream.(8)

In addition to work on immunologically active proteins, which as far as Bresler's work is concerned also has an important bearing on the structure and synthesis of proteins of any type irrespective of their immunological activity (1,2,), extensive research has apparently been conducted in the USSR on proteins which have specific enzyme activity and on the enzymatic activity of proteins in general. That this is the case is indicated by the papers given at a joint conference held on 19 November 1953 by the Institute of Biochemistry imeni A. N. Bakh, Academy of Sciences USSR, and the Institute of Plant Physiology imeni K. A. Timiryazev, Academy of Sciences USSR. According to the summary of a paper by V. L. Kretovich, included in the published report on this conference, the proteins stored by plants (e.g., the edestin of hemp seeds, the glycinin of soybeans, and the gliadin of wheat) stimulate the amination of pyruvic acid by ammonia to alanine. By applying

a special method for the isolation of proteins, which involves the use of low temperatures during extraction and dialysis and the drying of frozen protein preparations in vacuum, Kretovich obtained proteins possessing [illegible] diaphorase, dehydrogenase, peroxidase, catalase, and carboxylase activity, or the capacity to synthesize aspartic acid from ammonia and oxaloacetic acid or fumaric acid. On the other hand, when the commonly used Osborn method for the isolation of proteins is applied, the enzymatic activity of the proteins is largely or completely lost. For that reason the proteins stored by plants were assumed to be devoid of enzymatic activity prior to the work done by Kretovich. The preceding account of work done by Kretovich and his group is concluded with the statement that the results obtained in regard to the enzymatic activity of plant proteins are in agreement with the finding by V. A. Engel'gardt and M. N. Lyubimova, that muscle myosin acts as an enzyme. (9)

The question as to whether myosin and the plant proteins isolated by Kretovich would retain, after being hydrolyzed and subjected to Bresler's pressure resynthesis, any of the enzymatic properties which they may possess is of great interest in view of the fact that myogen, which Bresler on the basis of V. A. Engel'gardt's work apparently regards as being identical with muscle aldolase (4), loses most of its enzyme activity after this treatment.

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